AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for effecting an homologous recombination between a double-stranded native nucleic acid segment in a cell and a donor nucleic acid segment introduced into the cell, which method comprises the steps consisting of:

a) introducing into a cell a nucleic acid targeting system comprising:

(i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment,

(ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment so that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region,

(iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide,

b) allowing the third strand oligonucleotide to bind to the native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the native nucleic acid segment target region; and

c) allowing homologous recombination to occur between the native and donor nucleic acid segments;

wherein said donor nucleic acid is between more than 100 and 1,000,000 bases in length.

2. (Currently Amended) The method according to claim 1, wherein said donor nucleic acid is prepared by chemical synthesis ~~of~~ or by an amplification method.

3. (Original) The method according to claim 1, comprising the steps consisting of:

a) providing a pair of primers complementary of the 5' and 3' ends of a double-stranded first native nucleic acid sequence;

b) amplifying said first native nucleic acid sequence,

c) isolating the amplification product thus obtained;

d) annealing the amplification product with an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of the nucleotide sequence of said amplified nucleic acid through Watson-Crick base pairing, said adapter segment being linked to a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second native nucleic acid segment, thereby providing a nucleic acid targeting system comprising:

(i) said third strand oligonucleotide,

(ii) said amplification product as a donor nucleic acid segment, and

(iii) said adapter segment bound to said donor nucleic acid segment through Watson-Crick base pairing;

e) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;

f) allowing the third strand oligonucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and

g) allowing homologous recombination to occur between the second native and donor nucleic acid segments.

4. (Original) The method according to claim 1, wherein the donor nucleic acid is selected from the group consisting of a double-stranded nucleic acid, a substantially complementary pair of single stranded nucleic acids and a single stranded nucleic acid.

5. (Currently Amended) The method according to claim 1, comprising the steps consisting of:

a) providing a pair of primers complementary to the 5' and 3' ends of a first double-stranded native nucleic acid sequence, wherein one of the primers is an adapter segment linked to a third strand oligonucleotide that comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second double-stranded native nucleic acid segment;

b) amplifying said first native nucleic acid sequence,

c) isolating the amplification product thus obtained, thereby providing a nucleic acid targeting system comprising:

(i) said third strand oligonucleotide,

(ii) said amplification product as a donor nucleic acid segment, and

(iii) said adapter segment bound to a strand of said donor nucleic acid segment through Watson-Crick base pairing;

d) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;

e) allowing the nucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and

f) allowing homologous recombination to occur between the second native and donor nucleic acid segments.

6. (Original) The method according to claim 1 comprising the steps consisting of:

a) providing a pair of primers complementary to the 5' and 3' ends of a first double-stranded native nucleic acid sequence, wherein one of the primers is a modified adapter segment which contains one or several ribonucleotide(s) at its 3'-end, wherein said adapter segment is linked to a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a second double-stranded native nucleic acid segment;

b) amplifying said first native nucleic acid sequence,

c) isolating the amplification product thus obtained,

d) treating the isolated amplification product in conditions sufficient to allow destruction of said ribonucleotide, thereby providing a nucleic acid targeting system comprising:

(i) said third strand oligonucleotide,

(ii) said amplification product as a donor nucleic acid segment, and

(iii) said adapter segment bound to said donor nucleic acid segment through Watson-Crick base pairing;

e) introducing said nucleic acid targeting system into a cell comprising a second native nucleic acid different from the first native nucleic acid;

f) allowing the nucleotide to bind to the second native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the second native nucleic acid segment target region; and

g) allowing homologous recombination to occur between the second native and donor nucleic acid segments.

7. (Original) The method according to claim 6, wherein step d) comprises enzymatic or mild alkaline treatment.

8. (Currently amended) The method according to claim 1, wherein said third strand oligonucleotide is a single DNA molecule of between 7 and 50 nucleotides~~, preferably between 10 and 30 nucleotides~~.

9. (Currently amended) The method according to claim 1, wherein the donor nucleic acid is between ~~40~~ more than 100 and about ~~1,000,000~~ 3000 bases in length.

10. (Currently amended) The method according to claim 1, wherein the adapter is a single-stranded oligonucleotide comprising between 4 and 120 ~~preferably between 8 and 30~~ nucleotides.

11. (Original) The method according to claim 1, wherein the adapter is linked to said third strand oligonucleotide through a spacer.

12. (Currently amended) The method according to claim 1, wherein the spacer comprises a hydrocarbon skeleton ~~optionally interrupted or substituted by one or more heteroatoms, or heterogroups that comprise at least one of these heteroatoms~~.

13. (Original) The method according to claim 11, wherein the spacer comprises a polyethyleneglycol chain or a mixed structure comprising polyethyleneglycol units and (oligo) nucleotide units.

14. (Currently amended) The method according to claim 11, wherein the spacer is a ~~hexaethyleglycol~~ hexaethyleneglycol chain.

15. (Original) The method according to claim 1, wherein the native nucleic acid contains a mutation that is corrected by the homologous recombination.

16. (Original) The method according to claim 15, wherein the mutation is selected from the group consisting of base changes, deletions, insertions, nucleotide repeats, and combinations thereof.

17. (Original) The method according to claim 1, wherein the homologous recombination causes an alteration in the native nucleic acid sequence.

18. (Original) The method according to claim 17, wherein the alteration is caused in a segment selected from the group consisting of a gene, a part of a gene, a gene control region, an intron, a splice junction, a transposable element, a site specific recombination sequence, and combinations thereof.

19. (Original) The method according to claim 1, wherein the native nucleic acid is chromosomal.

20. (Original) The method according to claim 1, wherein the native nucleic acid is extrachromosomal.

21. (Original) The method according to claim 15, wherein the native nucleic acid is selected from the group consisting of mitochondrial DNA, episomal DNA, a plasmid and chloroplast DNA.

22. (Withdrawn) A kit comprising:

(i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment;

(ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment so that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region; and

(iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide.

23. (Original) A method for effecting gene alteration or mutation repair at a specific-sequence site on a native DNA, comprising:

a) introducing into a cell a nucleic acid targeting system comprising:

(i) a third strand oligonucleotide which comprises a base sequence capable of forming a triple helix at a binding region on one or both strands of a native nucleic acid segment,

(ii) a donor nucleic acid, comprising a nucleic acid sequence substantially homologous to the native nucleic acid segment such that the donor sequence is capable of undergoing homologous recombination with the native sequence at the target region,

(iii) an adapter segment comprising an oligonucleotide sequence able to bind at least a portion of said donor nucleic acid through Watson-Crick base pairing, the adapter segment being linked to said third strand oligonucleotide,

b) allowing the oligonucleotide to bind to the native nucleic acid segment to form a triple helix nucleic acid, thereby inducing homologous recombination at the native nucleic acid segment target region; and

c) allowing homologous recombination to occur between the native and donor nucleic acid segments,

thereby performing that gene alteration or mutation repair.

24. (New) The method according to claim 1, wherein said third strand oligonucleotide is a single DNA molecule of between 10 and 30 nucleotides.

25. (New) The method according to claim 1, wherein the adapter is a single-strand oligonucleotide comprising between 8 and 30 nucleotides.

26. (New) The method according to claim 12, wherein the hydrocarbon skeleton is interrupted and/or substituted by one or more heteroatoms, or heterogroups that comprise at least one of these heteroatoms.